UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAR 16 2006

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of Registrant Response to Deficiency Letter in Support of the Registration of B2E-07 (EPA Registration No. 75318-T), Containing 2.800% (S)-Methoprene [Isopropyl (2E,4E,7S)-methoxy-3,7,11-trimethyl-2,4-dodecadienoate] [redacted] Chemical No. 105402) As Its Active Ingredient. DP Barcode 326248; Decision No. 353329; MRID No. 46740101, 46721801, 46721803, 46721804.

FROM: Angela L. Gonzales, Biologist
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511C)

TO: Mari Duggard, Regulatory Action Leader
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511C)

ACTION REQUESTED

Technology Sciences Group, Inc. on the behalf of B2E Biotech LLC, requests registration of B2E-07 (EPA Reg. No. 75318-T), an end-use product (EP) containing 2.800% (S)-Methoprene [Isopropyl (2E,4E,7S)-methoxy-3,7,11-trimethyl-2,4-dodecadienoate], an insect growth regulator (IGR), as its active ingredient. [redacted] This product is intended to be sold in granular form for use to control mosquitoes, filter flies and non-biting midges in breeding areas. In support of registration, the registrant submitted a Confidential Statement of Formula (CSF) dated 11/13/04, a proposed product label, product chemistry data in MRIDs 46459201-46459204, efficacy data in MRIDs 46459205-46459207, and acute toxicity waiver rationale in MRID 46459208. Deficiencies regarding the submission were addressed in a letter from the Agency dated September 14, 2005, to which the registrant replied in a November 30, 2005 submission. This memorandum is a review of this submission.

~~THE FOLLOWING PAGES CONTAIN CONFIDENTIAL BUSINESS INFORMATION~~

RECOMMENDATIONS AND CONCLUSIONS

**Methoprene is exempt from the requirement of a tolerance in or on all food commodities when used to control insect larva. (40 CFR 180.1033)

Product Chemistry- ACCEPTABLE, pending resolution of deficiencies below.

1. The percentage of the TGAI on the label must be consistent with that on the CSF. The registrant must change the percent of the TGAI on the label from 2.8% to 2.800%.

Toxicology- ACCEPTABLE.

Ecotoxicology- ACCEPTABLE.

1. The submitted data establish (S)-methoprene concentrations at lesser levels than the lowest observed effect concentration (LOEC) of 2.0 ppb on Mysid shrimp (*Mysidopsis bahia*), determined by BPPD and discussed in a memorandum from A. L. Gonzales to M. Duggard dated February 17, 2005.

Efficacy- ACCEPTABLE, pending clarification of label language discussed in item #1 and inclusion of label language discussed in item #2 below.

1. Because efficacy testing was conducted using commercial application rates (lbs/acre) (see Sublabel A) and residential application rates are measured using "scoops" of product (see Sublabel B), the registrant must clarify the similarities between the two application types in terms of amount of product used on amount of surface area.

2. Based on the data submitted, B2E-07 applied at 2.5 lbs/acre or 5.0 lbs/acre is efficacious against *Ochlerotatus taeniorhynchus* mosquitoes for 35 days in water depths of up to 6 inches. A statement such as, "B2E-07 is effective in water depths of up to 6 inches" must be placed on the label.

Note: Two efficacy studies were submitted in support of registration of the EP. MRID 46740101 is classified as supplemental due to data deficiencies, which are listed below. MRID 46721803 is classified as acceptable and contains adequate data to support registration.

MRID 46740101-SUPPLEMENTAL

1. Replicates were not performed for the 2.5 lbs/acre and 5.0 lbs/acre test. One sample was collected from one test site and results were reported based on the data collected from the sample. Results cannot be validated from only one sample.

2. Mean water depths of the test sites must be submitted.

MRID 46721803- ACCEPTABLE

1. The submitted data demonstrate efficacy of B2E-07 at 2.5 lbs/acre or 5.0 lbs/acre against *Ochlerotatus taeniorhynchus* mosquitoes for 35 days in water depths of up to 6 inches.

NOTE TO RAL:

1. The statement on Sublabel B, "Apply additional granules as necessary to control larger areas" is too vague and is not supported by data.

STUDY SUMMARIES

Note: DERs were not prepared for the MRIDs. Submitted MRIDs are summarized below.

Product Chemistry (MRID 46721801)

The registrant's submission was adequate to resolve the deficiencies concerning the product chemistry data requirements. The spelling error for the inert ingredient [redacted] was corrected on the CSF. The CAS number for [redacted] was also corrected on the CSF. A revised manufacturing process with the correct amounts of ingredients was submitted and the registrant verified that the amounts of ingredients listed on the CSF correspond with those in the manufacturing process. [redacted]

Toxicology (MRID 46721801)

The registrant's discussion concerning the presence of respirable particles (fines) in the EP is adequate. [redacted] The registrant indicated that the process produces granules that do not break or disintegrate during packaging, shipping, storage or use.

Ecotoxicology (MRID 46721804)

Estimated Environmental Concentration (EEC) of (S)-Methoprene Determination

(S)-Methoprene concentrations were ascertained from B2E-07 applications to three test sites: 1) intermittent floodwater 2) permanent fresh water and 3) salt water tidal marsh. Initial location

sizes ranged from 4,860ft^2 to 23,085ft^2 with water depths averaging from 1.0ft to 3.0ft. The EP was applied once at each site at the maximum application rate (5.0 lbs/acre) according to label instructions. Two water samples were collected from each of two locations from each site at one hour before application, one hour after application and 24, 48, 72, 96, 120, 144 and 168 hours after application. Samples were extracted within two hours of collection using dichloromethane. Analysis of (S)-Methoprene concentrations was performed by capillary gas chromatography with flame ionization detection. Methods were validated with a 96.0% w/w (S)-Methoprene reference standard. Water quality samples (pre-treatment) were analyzed within two hours of collection for pH, hardness, alkalinity and total dissolved solids. Mean levels of the TGAI concentrations in each test site are presented in Table 1:

Table 1. Mean Concentrations of (S)-Methoprene in Test Sites*

Hours after application	Salt (μg/L)	Flood(μg/L)	Fresh (μg/L)	Mean[a] (μg/L)	Upper Limit[b](μg/L)
-1	0.53	--**	0.30	0.36	0.59
1	1.94	0.51	0.97	1.14	1.84
24	1.58	0.31	--	0.54	1.25
48	1.04	--	--	0.52	0.94
72	2.12	--	--	0.88	1.88
96	1.72	0.32	--	0.76	1.76
120	1.63	0.33	--	0.56	1.31
144	1.66	0.43	--	0.78	1.70
168	1.55	0.38	--	0.73	1.41

*Data reproduced from MRID 46721804

** -- = < 0.257μg/L, which is the minimum quantifiable level (used for mean calculations)

[a] Overall average of results from all sites

[b] Based on 95% Confidence Interval (P = 0.05) (using entire data set)

The overall average concentration of (S)-Methoprene was determined to be 1.14μg/L at the initiation of the study (one hour after application) and 0.73μg/L at the conclusion (168 hour post-treatment) of the study. Based on the data submitted, calculated concentrations of the TGAI are lower than the LOEC of 2.0 ppb (μg/L) for Mysid shrimp (*Mysidopsis bahia*), determined by BPPD and discussed in a memorandum from A. L. Gonzales to M. Duggard dated February 17, 2005.

Efficacy

MRID 46740101-SUPPLEMENTAL

B2E-07 was applied at rates from 2.5 lbs/acre to 10 lbs/acre to native irrigated pasture sites known to be mosquito breeding areas. For the purposes of this memorandum, the results from the application rates of 2.5 lbs/acre and 5.0 lbs/acre will be discussed because they are representative of label application rates. One site per application rate was tested during the study. For the 2.5 lbs/acre test, the site was treated post-hatch. A collection of 40 pupae was taken from the perimeter of the site and monitored in a cup until the completion of development 34 days later. The test resulted in a 97.5% IE. For the 5.0 lbs/acre test, the site was treated pre-hatch. The collection of a first brood of 40 pupae resulted in 100% IE, and a second hatch with

subsequent irrigation and collection resulted in 100% IE 46 days after treatment. Pupae development was recorded as either pupae dead in the cup, adult mosquitoes dead on the water, or adults that emerged and flew from the cup. To determine the number of adult mosquitoes that flew from the cup, pupal skins were counted and the number of dead adult mosquitoes subtracted from the number of pupal skins. Pupal collections from adjacent untreated mosquito breeding sites were made concurrently and used as controls. Control data demonstrated a 2.5% IE. Data were analyzed using a *Chi*-square test at 0.05 levels between control and treatment. Mean water depths of the sites were not reported. Raw data and calculations were not provided in the submission, but methods were referenced and data and calculations are available upon request. Replicates of each test were not performed.

MRID 46721803: ACCEPTABLE

B2E-07 was applied at 2.5 lbs/acre and 5.0 lbs/acre in uncovered concrete tanks within an outdoor screened enclosure. Three plots were utilized per application rate and three plots served as controls. Water depth measured approximately 6 inches with a salinity (added) of 3 to 5 ppt. The substrate in the plots was composed of about 6 inches of soil and emergent grasses. Around 800 laboratory reared mosquitoes (*Ochlerotatus taeniorhynchus*) were added to each plot. At least 100 pupae per plot were collected in cups after treatment and observed. After each pupal collection plots were drained and allowed to dry for a period of 7 to 10 days before re-flooding. Rainfall did not cause an overflow in any of the plots. pH measurements were adequate. Percent IE was calculated by the following formula:

$$\%IE = 100 - [(CS\text{-}DA)/(CS + PE + DP) \times 100]$$

CS = cast pupae skins
DP = dead pupae
PE = partially emerged adults
DA = dead adults

At 35 days, the control plot resulted in an average of 4.04% IE (each plot %IE: 6.20, 4.55, 1.48).

At 35 days at the application rate of 5.0 lbs/acre, an average of 99.26% IE was achieved (each plot %IE: 100.00, 97.84, 100.00).

At 35 days at the application rate of 2.5 lbs/acre, an average of 86.21% IE was achieved (each plot %IE: 58.33, 100.00, 99.25).

Percent IE was also determined at 7, 21, 48, 62, and 72 days. Acceptable %IE was only achieved for up to 35 days. Raw data and calculations were not reported, but are available upon request.

cc: A. Gonzales, M. Duggard, BPPD Subject File, IHAD/ARS
A. Gonzales, FT, CM2, 03/16/2006

13544

R153138

Chemical: S-Methoprene

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